D1 Cont ACCGGCCTTTCGCGGTGA or 5'-GTGCACGGAAAGGTGCAGGCCACACT (SEQ ID NOS: 24-26).

➢ On Page 47, please replace lines 13-18 with the following text:

In an exemplary embodiment, portions of the 5' flanking region of the human Shh gene are amplified using primers which add restriction sites, to generate the following fragments

D2 5'-gcgcgcttcgaaGCGAGGCAGCCAGCGAGGGAGAGAGCGAGCGGGCGAGCCGGAGC-GAGGAAatcgatgcgcgc (primer 1) (SEQ ID NO: 21)

5'-gcgcgcagatctGGGAAAGCGCAAGAGAGAGCGCACACGCACACACCCGCCGCGCG-CACTCGggatccgcgcgc (primer 2) (SEQ ID NO: 22)

➢ On Page 48, please replace lines 1-20 with the following text:

Individual colonies are selected, cut with AsuII and BamHI, and the size of the AsuII/BamHI fragment determined. Colonies in which both the primer-1 and primer-2 sequences are correctly inserted are further amplified, and cut with AsuII and BamHI to produce the gene activation construct:

cgaagcgaggcagccagcgagggagagagcgagcgggcgagccggagcgaggaaATCGAAGGTT
CGAATCCTTCCCCCACCACCATCACTTTCAAAAGTCCGAAAGAATCTGCTCCCTGCTTGTGTGT
TGGAGGTCGCTGAGTAGTGCGCGAGTAAAATTTAAGCTACAACAAGGCAAGGCTTGACCGACAA
TTGCATGAAGAATCTGCTTAGGGTTAGGCGTTTTGCGCTGCTTCGCGATGTACGGGCCAGATAT
ACGCGTTGACATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATA
GCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAA
D3 CGACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTC
CATTGACGTCAATGGGTGGACTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATC
ATATGCCAAGTACGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCA
GTACATGACCTTATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACC
ATGGTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTC
CAAGTCTCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCC
AAAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTC
TATATAAGCAGAGCTCTCTGGCTAACTAGAGAACCCACTGCTTACTGGCTTATCGAAATTAATA
CGACTCACTATAGGGAGACCCAAGCTTGGTACCGAGCTCGGATCgatctgggaaagcgcaagag
agagcgcacacgcacacacccgccgcgcgcactcgg (SEQ ID NO: 23)

➢ On Page 62, please replace lines 16-21 with the following text:

In an illustrative embodiment, the ptc therapeutic can be an antisense construct for inhibiting the expression of *patched*, e.g., to mimic the inhibition of *patched* by *hedgehog*. Exemplary antisense constructs include:

D4

5'-GTCCTGGCGCCGCCGCCGCCGTCGCC (SEQ ID NO: 24)

5'-TTCCGATGACCGGCCTTTCGCGGTGA (SEQ ID NO: 25)

5'-GTGCACGGAAAGGTGCAGGCCACACT (SEQ ID NO: 26)

The replacement paragraphs presented above incorporates changes as indicated by the marked-up versions below.

In yet other embodiments of the present invention, the *ptc* therapeutic alters the level of expression of a *hedgehog* protein, a patched protein or another protein involved in the intracellular signal transduction pathway of *patched*. In this regard, the *ptc* therapeutic can be an antisense construct which inhibits the expression of a protein which is involved in the signal transduction pathway of *patched* and the expression of which antagonizes *hedgehog*-mediated signals. For example, the antisense molecule can be one which hyridizes to a *patched* transcript or genomic sequence, such as 5'-GTCCTGGCGCCGCCGCCGCCGTCGCC, 5'-TTCCGATG-ACCGGCCTTTCGCGGTGA or 5'-GTGCACGGAAAGGTGCAGGCCACACT (SEQ ID NOS: 24-26).

In an exemplary embodiment, portions of the 5' flanking region of the human Shh gene are amplified using primers which add restriction sites, to generate the following fragments

5′-gcgcgcttcgaaGCGAGGCAGCCAGCGAGGGAGAGAGCGAGCGGGCGAGCCGGAGC-GAGGAAatcgatgcgcgc (primer 1) (SEQ ID NO: 21)

5′-gcgcgcagatctGGGAAAGCGCAAGAGAGAGCGCACACGCACACACCCGCCGCGCG-CACTCGggatccgcgcgc (primer 2) (SEQ ID NO: 22)

Individual colonies are selected, cut with AsuII and BamHI, and the size of the AsuII/BamHI fragment determined. Colonies in which both the primer 1 and primer 2 sequences

are correctly inserted are further amplified, and cut with AsuII and BamHI to produce the gene activation construct:

cgaagcgaggcagccagcgagggagagagcgagcgggcgagccggagcgaggaaATCGAAGGTT
CGAATCCTTCCCCCACCACCATCACTTTCAAAAGTCCGAAAGAATCTGCTCCCTGCTTGTGTGT
TGGAGGTCGCTGAGTAGTGCGCGAGTAAAATTTAAGCTACAACAAGGCAAGGCTTGACCGACAA
TTGCATGAAGAATCTGCTTAGGGTTAGGCGTTTTGCGCTGCTTCGCGATGTACGGGCCAGATAT
ACGCGTTGACATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATA
GCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAA
CGACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTC
CATTGACGTCAATGGGTGGACTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATC
ATATGCCAAGTACGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCA
GTACATGACCTTATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACC
ATGGTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTC
CAAGTCTCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCC
AAAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTC
TATATAAGCAGAGCTCTCTGGCTAACTAGAGAACCCACTGCTTACTGGCTTATCGAAATTAATA
CGACTCACTATAGGGAGACCCAAGCTTGGTACCGAGCTCGGATCgatctgggaaagcgcaagag
agagcgcacacgcacacacccgccgcgcgcactcgg (SEQ ID NO: 23)

In an illustrative embodiment, the ptc therapeutic can be an antisense construct for inhibiting the expression of *patched*, e.g., to mimic the inhibition of *patched* by *hedgehog*. Exemplary antisense constructs include:

5'-GTCCTGGCGCCGCCGCCGCCGTCGCC (SEQ ID NO: 24)

5'-TTCCGATGACCGGCCTTTCGCGGTGA (SEQ ID NO: 25)

5'-GTGCACGGAAAGGTGCAGGCCACACT (SEQ ID NO: 26)

IN THE CLAIMS:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.